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* * * * * * * * * *   Welcome to STN International   * * * * * * * * * *

 NEWS  1          Web Page for STN Seminar Schedule - N. America
 NEWS  2  APR 02  CAS Registry Number Crossover Limits Increased to
                  500,000 in Key STN Databases
 NEWS  3  APR 02  PATDPAFULL: Application and priority number formats
                  enhanced
 NEWS  4  APR 02  DWPI: New display format ALLSTR available
 NEWS  5  APR 02  New Thesaurus Added to Derwent Databases for Smooth
                  Sailing through U.S. Patent Codes
 NEWS  6  APR 02  EMBASE Adds Unique Records from MEDLINE, Expanding
                  Coverage back to 1948
 NEWS  7  APR 07  50,000 World Traditional Medicine (WTM) Patents Now
                  Available in CAplus
 NEWS  8  APR 07  MEDLINE Coverage Is Extended Back to 1947
 NEWS  9  JUN 16  WPI First View (File WPIFV) will no longer be
                  available after July 30, 2010
 NEWS 10  JUN 18  DWPI: New coverage - French Granted Patents
 NEWS 11  JUN 18  CAS and FIZ Karlsruhe announce plans for a new
                  STN platform
 NEWS 12  JUN 18  IPC codes have been added to the INSPEC backfile
                  (1969-2009)
 NEWS 13  JUN 21  Removal of Pre-IPC 8 data fields streamline displays
                  in CA/CAplus, CASREACT,and MARPAT
 NEWS 14  JUN 21  Access an additional 1.8 million records exclusively
                  enhanced with 1.9 million CAS Registry Numbers --
                  EMBASE Classic on STN
 NEWS 15  JUN 28  Introducing "CAS Chemistry Research Report": 40 Years
                  of Biofuel Research Reveal China Now Atop U.S. in
                  Patenting and Commercialization of Bioethanol
 NEWS 16  JUN 29  Enhanced Batch Search Options in DGENE, USGENE,
                  and PCTGEN
 NEWS 17  JUL 19  Enhancement of citation information in INPADOC
                  databases provides new, more efficient competitor
                  analyses
 NEWS 18  JUL 26  CAS coverage of global patent authorities has
                  expanded to 61 with the addition of Costa Rica
 NEWS 19  SEP 15  MEDLINE Cited References provide additional
                  revelant records with no additional searching.
 NEWS 20  OCT 04  Removal of Pre-IPC 8 data fields streamlines
                  displays in USPATFULL, USPAT2, and USPATOLD.
 NEWS 21  OCT 04  Precision of EMBASE searching enhanced with new
                  chemical name field
 NEWS 22  OCT 06  Increase your retrieval consistency with new formats for
                  Taiwanese application numbers in CA/CAplus.

 NEWS EXPRESS FEBRUARY 15 10 CURRENT WINDOWS VERSION IS V8.4.2,
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  and other penalties.

* * * * * * * * * * * * * * STN  Columbus  * * * * * * * * * * * * * * *

FILE 'HOME' ENTERED AT 14:17:33 ON 07 OCT 2010

=> file registry
COST IN U.S. DOLLARS                             SINCE FILE      TOTAL
                                                      ENTRY    SESSION
FULL ESTIMATED COST                                    0.22       0.22

FILE 'REGISTRY' ENTERED AT 14:17:46 ON 07 OCT 2010
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provided by InfoChem.

STRUCTURE FILE UPDATES:    6 OCT 2010  HIGHEST RN 1245698-26-3
DICTIONARY FILE UPDATES:   6 OCT 2010  HIGHEST RN 1245698-26-3

New CAS Information Use Policies, enter HELP USAGETERMS for details.

TSCA INFORMATION NOW CURRENT THROUGH June 26, 2010.

  Please note that search-term pricing does apply when
  conducting SmartSELECT searches.

REGISTRY includes numerically searchable data for experimental and
predicted properties as well as tags indicating availability of
experimental property data in the original document.  For information
on property searching in REGISTRY, refer to:

http://www.cas.org/support/stngen/stndoc/properties.html

=> s cyclopamine
L1          10 CYCLOPAMINE

=> file caplus
COST IN U.S. DOLLARS                             SINCE FILE      TOTAL
                                                      ENTRY    SESSION
FULL ESTIMATED COST                                    5.99       6.21

FILE 'CAPLUS' ENTERED AT 14:17:55 ON 07 OCT 2010
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FILE COVERS 1907 - 7 Oct 2010  VOL 153 ISS 15
FILE LAST UPDATED: 6 Oct 2010  (20101006/ED)
REVISED CLASS FIELDS (/NCL) LAST RELOADED:  Aug 2010
USPTO MANUAL OF CLASSIFICATIONS THESAURUS ISSUE DATE:  Aug 2010

CAplus now includes complete International Patent Classification (IPC)
reclassification data for the third quarter of 2010.

CAS Information Use Policies apply and are available at:

http://www.cas.org/legal/infopolicy.html

This file contains CAS Registry Numbers for easy and accurate
substance identification.

=> s l1
L2         294 L1

=> s l2 and (cancer or tumor or neoplasm)
        476098 CANCER
         69908 CANCERS
        493171 CANCER
                 (CANCER OR CANCERS)
        564400 TUMOR
        201049 TUMORS
        625336 TUMOR
                 (TUMOR OR TUMORS)
          5086 TUMOUR
          1910 TUMOURS
          6869 TUMOUR
                 (TUMOUR OR TUMOURS)
        625787 TUMOR
                 (TUMOR OR TUMOUR)
        621055 NEOPLASM
         39194 NEOPLASMS
        638568 NEOPLASM
                 (NEOPLASM OR NEOPLASMS)
L3         160 L2 AND (CANCER OR TUMOR OR NEOPLASM)

=> s l3 and apoptosis
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             1 APOPTOSISES
        218328 APOPTOSIS
                 (APOPTOSIS OR APOPTOSISES)
L4          48 L3 AND APOPTOSIS

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                 (PD<20010702)
L5           2 L4 AND PD<20010702

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PROCESSING COMPLETED FOR L5
L6            2 DUP REM L5 (0 DUPLICATES REMOVED)

=> d l6 1-2 ibib abs

L6   ANSWER 1 OF 2  CAPLUS  COPYRIGHT 2010 ACS on STN
ACCESSION NUMBER:        2007:41409  CAPLUS
DOCUMENT NUMBER:         146:135532
TITLE:                   Methods and compositions for inhibiting tumorigenesis
                         using siRNA to inhibit hedgehog and Gli signaling
                         pathway
INVENTOR(S):             Ruiz Altaba, Ariel; Stecca, Barbara
PATENT ASSIGNEE(S):      USA
SOURCE:                  U.S. Pat. Appl. Publ., 135pp., Cont.-in-part of U.S.
                         Ser. No. 930,723.
                         CODEN: USXXCO
DOCUMENT TYPE:           Patent
LANGUAGE:                English
FAMILY ACC. NUM. COUNT:  5
PATENT INFORMATION:

     PATENT NO.          KIND   DATE        APPLICATION NO.        DATE
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     US 20070009530       A1    20070111    US 2006-407702         20060420
     US 7709454           B2    20100504
     US 6238876           B1    20010529    US 1998-102491         19980622 <--
     US 20030100032       A1    20030529    US 2001-825155         20010403
     US 20040092010       A1    20040513    US 2003-414267         20030415
     US 20040072345       A1    20040415    US 2003-456954         20030606
     US 20050130922       A1    20050616    US 2004-927951         20040829
     US 20050112707       A1    20050526    US 2004-930723         20040831
     US 7741298           B2    20100622
PRIORITY APPLN. INFO.:                      US 1997-50286P      P  19970620
                                            US 1998-102491      A1 19980622
                                            US 2001-825155      B2 20010403
                                            US 2002-372508P     P  20020415
                                            US 2003-414267      B2 20030415
                                            US 2003-456954      A2 20030606
                                            US 2004-927951      A2 20040829
                                            US 2004-930723      A2 20040831
AB   The present invention relates to compds., small interfering RNAs and
     compns. and methods of inhibiting tumorigenesis and methods of inhibiting
     tumor cell growth and proliferation using agents that inhibit the
     hedgehog and Gli signaling pathway, including agents that inhibit GLI
     synthesis and function.  The present invention also relates to particular
     biomarkers that can be used in the diagnosis and prognosis of melanomas.
     Methods of treating cancer, including melanoma are also provided
     using small organic compds., siRNAs and blocking antibodies that inhibit or
     block the SHH/GLI pathway.  In addition, the use of agents that inhibit other
     signaling pathways is contemplated for use as second agents to be used in
     conjunction with the inhibitors of the GLI pathway.  The antagonist is a
     small mol. inhibitor of GLI expression, synthesis or activity, such as
     plant alkaloid selected from cyclopamine, jervine, or their analogs.
OS.CITING REF COUNT:     4     THERE ARE 4 CAPLUS RECORDS THAT CITE THIS RECORD
                               (4 CITINGS)
REFERENCE COUNT:         100   THERE ARE 100 CITED REFERENCES AVAILABLE FOR
                               THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE
                               FORMAT

L6   ANSWER 2 OF 2  CAPLUS  COPYRIGHT 2010 ACS on STN
ACCESSION NUMBER:        2005:450836  CAPLUS
DOCUMENT NUMBER:         143:19953
```

```
TITLE:                   SHH/GLI pathway-based methods and compositions for
                         treatment and diagnosis of cancer
INVENTOR(S):             Ruiz i Altaba, Ariel; Sanchez, Pilar; Rom, William;
                         Wong, Kam-Meng Tchou
PATENT ASSIGNEE(S):      USA
SOURCE:                  U.S. Pat. Appl. Publ., 95 pp., Cont.-in-part of U.S.
                         Ser. No. 456,954.
                         CODEN: USXXCO
DOCUMENT TYPE:           Patent
LANGUAGE:                English
FAMILY ACC. NUM. COUNT:  5
PATENT INFORMATION:

     PATENT NO.          KIND   DATE       APPLICATION NO.        DATE
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     US 20050112707       A1    20050526   US 2004-930723         20040831
     US 7741298           B2    20100622
     US 6238876           B1    20010529   US 1998-102491         19980622 <--
     US 20030100032       A1    20030529   US 2001-825155         20010403
     US 20040092010       A1    20040513   US 2003-414267         20030415
     US 20040072345       A1    20040415   US 2003-456954         20030606
     US 20050130922       A1    20050616   US 2004-927951         20040829
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PRIORITY APPLN. INFO.:                     US 1997-50286P      P  19970620
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                                           US 2003-414267      A2 20030415
                                           US 2003-456954      A2 20030606
                                           US 2004-927951      A2 20040829
                                           US 2004-930723      A2 20040831
ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT
AB   The invention discloses compds., small interfering RNAs and compns. and
     methods of inhibiting tumorigenesis using agents that inhibit the sonic
     hedgehog and GLI signaling pathway, including agents that inhibit GLI
     expression, synthesis and/or function.  The invention also relates to
     particular biomarkers that can be used in the diagnosis and prognosis of
     cancer.  Methods of treating cancer, including
     glioblastomas, medulloblastomas, basal cell carcinomas, prostate
     cancer and small cell and non-small cell lung cancer are
     also provided using small organic compds., siRNAs and blocking antibodies
     that inhibit or block the SHH/GLI pathway.
OS.CITING REF COUNT:     1      THERE ARE 1 CAPLUS RECORDS THAT CITE THIS RECORD
                                (1 CITINGS)
REFERENCE COUNT:         83     THERE ARE 83 CITED REFERENCES AVAILABLE FOR THIS
                                RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT


=> d his

     (FILE 'HOME' ENTERED AT 14:17:33 ON 07 OCT 2010)

     FILE 'REGISTRY' ENTERED AT 14:17:46 ON 07 OCT 2010
L1           10 S CYCLOPAMINE

     FILE 'CAPLUS' ENTERED AT 14:17:55 ON 07 OCT 2010
L2          294 S L1
L3          160 S L2 AND (CANCER OR TUMOR OR NEOPLASM)
L4           48 S L3 AND APOPTOSIS
L5            2 S L4 AND PD<20010702
L6            2 DUP REM L5 (0 DUPLICATES REMOVED)
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       4104506 AD<20010702
                 (AD<20010702)
L7          10 L3 AND AD<20010702

=> dup rem l7
PROCESSING COMPLETED FOR L7
L8           10 DUP REM L7 (0 DUPLICATES REMOVED)

=> d l8 1-10 ibib abs

L8   ANSWER 1 OF 10  CAPLUS  COPYRIGHT 2010 ACS on STN
ACCESSION NUMBER:         2007:41409  CAPLUS
DOCUMENT NUMBER:          146:135532
TITLE:                    Methods and compositions for inhibiting tumorigenesis
                          using siRNA to inhibit hedgehog and Gli signaling
                          pathway
INVENTOR(S):              Ruiz Altaba, Ariel; Stecca, Barbara
PATENT ASSIGNEE(S):       USA
SOURCE:                   U.S. Pat. Appl. Publ., 135pp., Cont.-in-part of U.S.
                          Ser. No. 930,723.
                          CODEN: USXXCO
DOCUMENT TYPE:            Patent
LANGUAGE:                 English
FAMILY ACC. NUM. COUNT:   5
PATENT INFORMATION:

     PATENT NO.          KIND   DATE       APPLICATION NO.        DATE
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     US 20070009530       A1    20070111   US 2006-407702         20060420
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                                           US 2003-456954      A2 20030606
                                           US 2004-927951      A2 20040829
                                           US 2004-930723      A2 20040831
AB   The present invention relates to compds., small interfering RNAs and
     compns. and methods of inhibiting tumorigenesis and methods of inhibiting
     tumor cell growth and proliferation using agents that inhibit the
     hedgehog and Gli signaling pathway, including agents that inhibit GLI
     synthesis and function.  The present invention also relates to particular
     biomarkers that can be used in the diagnosis and prognosis of melanomas.
     Methods of treating cancer, including melanoma are also provided
     using small organic compds., siRNAs and blocking antibodies that inhibit or
     block the SHH/GLI pathway.  In addition, the use of agents that inhibit other
     signaling pathways is contemplated for use as second agents to be used in
     conjunction with the inhibitors of the GLI pathway.  The antagonist is a
     small mol. inhibitor of GLI expression, synthesis or activity, such as
     plant alkaloid selected from cyclopamine, jervine, or their analogs.
OS.CITING REF COUNT:     4     THERE ARE 4 CAPLUS RECORDS THAT CITE THIS RECORD
                               (4 CITINGS)
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REFERENCE COUNT:         100   THERE ARE 100 CITED REFERENCES AVAILABLE FOR
                               THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE
                               FORMAT

L8   ANSWER 2 OF 10  CAPLUS  COPYRIGHT 2010 ACS on STN
ACCESSION NUMBER:        2005:527384  CAPLUS
DOCUMENT NUMBER:         143:53470
TITLE:                   Compositions of small interfering RNAs for inhibiting
                         hedgehog and Gli signaling pathway and uses for
                         cancer therapy
INVENTOR(S):             Ruiz i Altaba, Ariel; Datta, Suma; Datta, Milton
PATENT ASSIGNEE(S):      USA
SOURCE:                  U.S. Pat. Appl. Publ., 95 pp., Cont.-in-part of U.S.
                         Ser. No. 456,954.
                         CODEN: USXXCO
DOCUMENT TYPE:           Patent
LANGUAGE:                English
FAMILY ACC. NUM. COUNT:  5
PATENT INFORMATION:

     PATENT NO.          KIND   DATE       APPLICATION NO.        DATE
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     US 20050130922       A1    20050616   US 2004-927951         20040829
     US 6238876           B1    20010529   US 1998-102491         19980622 <--
     US 20030100032       A1    20030529   US 2001-825155         20010403 <--
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     US 20040072345       A1    20040415   US 2003-456954         20030606
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     US 7741298           B2    20100622
     US 20070009530       A1    20070111   US 2006-407702         20060420
     US 7709454           B2    20100504
PRIORITY APPLN. INFO.:                     US 1997-50286P      P  19970620
                                           US 1998-102491      A1 19980622
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                                           US 2003-414267      A2 20030415
                                           US 2003-456954      A2 20030606
                                           US 2004-927951      A2 20040829
                                           US 2004-930723      A2 20040831
AB   The present invention relates to compds., small interfering RNAs and
     compns. and methods of inhibiting tumorigenesis and methods of inhibiting
     tumor cell growth and proliferation using agents that inhibit the
     hedgehog and Gli signaling pathway, including agents that inhibit GLI
     synthesis and/or function.  The present invention also relates to
     particular biomarkers that can be used in the diagnosis and prognosis of
     prostate cancer.  Methods of treating cancer,
     including prostate cancer are also provided using small organic
     compds., siRNAs and blocking antibodies that inhibit or block the SHH/GLI
     pathway.
OS.CITING REF COUNT:     2     THERE ARE 2 CAPLUS RECORDS THAT CITE THIS RECORD
                               (2 CITINGS)

L8   ANSWER 3 OF 10  CAPLUS  COPYRIGHT 2010 ACS on STN
ACCESSION NUMBER:        2005:450836  CAPLUS
DOCUMENT NUMBER:         143:19953
TITLE:                   SHH/GLI pathway-based methods and compositions for
                         treatment and diagnosis of cancer
INVENTOR(S):             Ruiz i Altaba, Ariel; Sanchez, Pilar; Rom, William;
                         Wong, Kam-Meng Tchou
PATENT ASSIGNEE(S):      USA
SOURCE:                  U.S. Pat. Appl. Publ., 95 pp., Cont.-in-part of U.S.
                         Ser. No. 456,954.
                         CODEN: USXXCO
DOCUMENT TYPE:           Patent
LANGUAGE:                English
FAMILY ACC. NUM. COUNT:  5
PATENT INFORMATION:

     PATENT NO.          KIND   DATE       APPLICATION NO.        DATE
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     US 20050112707       A1    20050526   US 2004-930723         20040831
     US 7741298           B2    20100622
     US 6238876           B1    20010529   US 1998-102491         19980622 <--
     US 20030100032       A1    20030529   US 2001-825155         20010403 <--
     US 20040092010       A1    20040513   US 2003-414267         20030415
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ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT
AB   The invention discloses compds., small interfering RNAs and compns. and
     methods of inhibiting tumorigenesis using agents that inhibit the sonic
     hedgehog and GLI signaling pathway, including agents that inhibit GLI
     expression, synthesis and/or function.  The invention also relates to
     particular biomarkers that can be used in the diagnosis and prognosis of
     cancer.  Methods of treating cancer, including
     glioblastomas, medulloblastomas, basal cell carcinomas, prostate
     cancer and small cell and non-small cell lung cancer are
     also provided using small organic compds., siRNAs and blocking antibodies
     that inhibit or block the SHH/GLI pathway.
OS.CITING REF COUNT:     1     THERE ARE 1 CAPLUS RECORDS THAT CITE THIS RECORD
                               (1 CITINGS)
REFERENCE COUNT:         83    THERE ARE 83 CITED REFERENCES AVAILABLE FOR THIS
                               RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8   ANSWER 4 OF 10  CAPLUS  COPYRIGHT 2010 ACS on STN
ACCESSION NUMBER:        2005:220113  CAPLUS
DOCUMENT NUMBER:         142:291381
TITLE:                   Hedgehog protein as angiogenesis-modulator and
                         therapeutic uses thereof
INVENTOR(S):             Ling, Leona E.; Sanicola-Nadel, Michele; Kotkow,
                         Karen; Rubin, Lee L.
PATENT ASSIGNEE(S):      USA
SOURCE:                  U.S. Pat. Appl. Publ., 113 pp., Cont.-in-part of U.S.
                         Ser. No. 883,848.
                         CODEN: USXXCO
DOCUMENT TYPE:           Patent
LANGUAGE:                English
FAMILY ACC. NUM. COUNT:  7
PATENT INFORMATION:

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                                            US 2000-688018      A3 20001013
ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT
OTHER SOURCE(S):         MARPAT 142:291381
AB   The present invention relates to the use of hedgehog protein, DNA, or
     other hedgehog therapeutic as an agent to induce the growth of new blood
     vessels, angiogenesis, arteriogenesis or vascular growth in adult tissues
     where the induction of angiogenesis has therapeutic value.  The present
     invention also relates to the use of inhibitors of hedgehog protein or
     signaling to prevent angiogenesis contributing to pathol. conditions such
     as neoplasia (tumors and gliomas), diabetic retinopathy,
     rheumatoid arthritis, osteoarthritis, macular degeneration, psoriasis,
     ulcerative colitis, Crohn's disease, and inflammation.  Hedgehog agonists
     and antagonists can be used to regulate angiogenesis, and have utility in
     treating tissue repair and cancer, and to prevent angiogenesis
     driven pathologies.
OS.CITING REF COUNT:     5     THERE ARE 5 CAPLUS RECORDS THAT CITE THIS RECORD
                               (9 CITINGS)
REFERENCE COUNT:         169   THERE ARE 169 CITED REFERENCES AVAILABLE FOR
                               THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE
                               FORMAT

L8   ANSWER 5 OF 10  CAPLUS  COPYRIGHT 2010 ACS on STN
ACCESSION NUMBER:        2004:310777  CAPLUS
DOCUMENT NUMBER:         140:318752
TITLE:                   Sonic hedgehog proteins regulating neurogenesis and
                         regulation of SHH/GLI signaling for neurodegenerative
                         disease and cancer therapies
INVENTOR(S):             Ruiz i Altaba, Ruiz I.; Sanchez, Maria Pilar
PATENT ASSIGNEE(S):      USA
SOURCE:                  U.S. Pat. Appl. Publ., 59 pp., Cont.-in-part of U.S.
                         Ser. No. 414,267.
                         CODEN: USXXCO
DOCUMENT TYPE:           Patent
LANGUAGE:                English
FAMILY ACC. NUM. COUNT:  5
PATENT INFORMATION:

     PATENT NO.          KIND   DATE        APPLICATION NO.        DATE
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     US 20070009530       A1    20070111    US 2006-407702         20060420
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PRIORITY APPLN. INFO.:                      US 1997-50286P      P  19970620
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                                        US 2003-456954      A2 20030606
                                        US 2004-927951      A2 20040829
                                        US 2004-930723      A2 20040831
ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT
AB   The present invention discloses methods of producing neuronal cells from
     stem cells, particularly from adult brain stem cells.  The use of such
     neuronal cells in the treatment and/or prevention of neurol. diseases,
     conditions and/or injuries is also disclosed.  In addition, the present
     invention provides a novel source of neuronal cells for use as a laboratory
     tool.  Sonic Hedgehog regulated SVZ neurogenesis in the postnatal and
     adult brain.  Gli2 mutant mice had reduced dorsal brain structures and
     germinative zones.  Gli2 mutant mice and shh mutant cortices produced few
     and small neurospheres.  Gli2 mutant cortices showed the loss of Gli1 and
     a reduction in Gli3 and neuroD expression.  Exptl. results suggested a
     required synergism of SHH and EGF for nsp formation and proliferation by
     neural stem cells.  Gene expression analyses with sorted SVZ cells and
     nsps suggested that SVZ astrocytes and possibly transiently amplifying
     precursors respond to SHH.  Exptl. findings suggest that SHH acts on
     amplifying precursors (C cells) to increase their proliferation and thus
     to increase the rate of neurogenesis.  Both the U87 glioblastoma cells, as
     well as the primary glioblastoma cells, when transfected with small
     inhibitory RNA mols. specific for Gli1, showed significant inhibition in
     proliferative capacity, as compared to control cells.
OS.CITING REF COUNT:     1     THERE ARE 1 CAPLUS RECORDS THAT CITE THIS RECORD
                               (1 CITINGS)

L8   ANSWER 6 OF 10  CAPLUS  COPYRIGHT 2010 ACS on STN
ACCESSION NUMBER:         2001:507523  CAPLUS
DOCUMENT NUMBER:          135:87198
TITLE:                    Use of steroidal alkaloids to reverse multidrug
                          resistance
INVENTOR(S):              Liscovitch, Mordechai; Lavie, Yaakov
PATENT ASSIGNEE(S):       Yeda Research and Development Co. Ltd., Israel
SOURCE:                   PCT Int. Appl., 31 pp.
                          CODEN: PIXXD2
DOCUMENT TYPE:            Patent
LANGUAGE:                 English
FAMILY ACC. NUM. COUNT:   1
PATENT INFORMATION:

     PATENT NO.          KIND   DATE       APPLICATION NO.        DATE
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     WO 2001049279        A2    20010712   WO 2000-IL866          20001228 <--
     WO 2001049279        A3    20021017
         W:  AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,
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             HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT,
             LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU,
             SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN,
             YU, ZA, ZW
         RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY,
             DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF,
             BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG
     CA 2395642           A1    20010712   CA 2000-2395642        20001228 <--
     EP 1274445           A2    20030115   EP 2000-983471         20001228 <--
     EP 1274445           B1    20050914
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     JP 2003519178        T     20030617   JP 2001-549647         20001228 <--
     AT 304360            T     20050915   AT 2000-983471         20001228 <--
     IL 149913            A     20060801    IL 2000-149913         20001228 <--
     US 20030114393       A1    20030619    US 2002-169353         20021104
PRIORITY APPLN. INFO.:                      IL 1999-133809      A  19991230
                                            WO 2000-IL866       W  20001228
ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT
AB   The invention provides steroidal alkaloids for inhibiting or reversing
     multidrug resistance in cancer or in bacterial, fungal or
     parasitic infections.  The steroidal alkaloid may be administered to the
     patient alone or in combination with an anticancer, antibacterial,
     antifungal or antiparasitic agent.  Examples of steroidal alkaloids
     include members of the solanidane or spirosolane families (e.g.
     tomatidine), and C-nor-D-homo steroids, e.g. of the jervane or veratramine
     families.
OS.CITING REF COUNT:     5     THERE ARE 5 CAPLUS RECORDS THAT CITE THIS RECORD
                               (5 CITINGS)
REFERENCE COUNT:         5     THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS
                               RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8   ANSWER 7 OF 10  CAPLUS  COPYRIGHT 2010 ACS on STN
ACCESSION NUMBER:        2001:283977  CAPLUS
DOCUMENT NUMBER:         134:295995
TITLE:                   Synthesis, compositions and uses of steroidal
                         alkaloids as regulators of the hedgehog pathway
INVENTOR(S):             Beachy, Philip A.
PATENT ASSIGNEE(S):      Johns Hopkins University School of Medicine, USA
SOURCE:                  PCT Int. Appl., 164 pp.
                         CODEN: PIXXD2
DOCUMENT TYPE:           Patent
LANGUAGE:                English
FAMILY ACC. NUM. COUNT:  1
PATENT INFORMATION:

     PATENT NO.          KIND   DATE        APPLICATION NO.        DATE
     ---------------     ----   --------    --------------------   --------
     WO 2001027135        A2    20010419    WO 2000-US28479        20001013 <--
     WO 2001027135        A3    20020510
     WO 2001027135        A9    20020815
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             HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT,
             LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU,
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     CA 2386190           A1    20010419    CA 2000-2386190        20001013 <--
     CA 2386190           C     20090414
     EP 1235851           A2    20020904    EP 2000-973544         20001013 <--
     EP 1235851           B1    20060531
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     JP 2003516317        T     20030513    JP 2001-530353         20001013 <--
     AU 781524            B2    20050526    AU 2001-12045          20001013 <--
     AT 328002            T     20060615    AT 2000-973544         20001013 <--
     US 7098196           B1    20060829    US 2000-688076         20001013 <--
     EP 1728797           A2    20061206    EP 2006-11086          20001013 <--
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     IL 149069            A     20070308    IL 2000-149069         20001013 <--
     US 20060128639       A1    20060615    US 2006-338503         20060123
     US 7476661           B2    20090113
     AU 2006202843        A1    20060803    AU 2006-202843         20060703
     AU 2006202843        B2    20090820
     US 20080255059       A1    20081016    US 2008-79776          20080328
PRIORITY APPLN. INFO.:                      US 1999-159215P     P  19991013
                                            US 2000-229273P     P  20000830
                                            AU 2001-12045       A3 20001013
                                            EP 2000-973544      A3 20001013
                                            US 2000-688076      A1 20001013
                                            WO 2000-US28479     W  20001013
                                            US 2006-338503      A1 20060123
ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT
OTHER SOURCE(S):         MARPAT 134:295995
AB   The present invention makes available, inter alia, methods and reagents
     for modulating smoothened-dependent pathway activation.  In certain
     embodiments, the subject methods can be used to counteract the phenotypic
     effects of unwanted activation of a hedgehog pathway, such as resulting
     from hedgehog gain-of-function, ptc loss-of-function or smoothened
     gain-of-function mutations.  Synthesis of cyclopamine, jervine and
     cycloposine derivs. is presented.
OS.CITING REF COUNT:     9     THERE ARE 9 CAPLUS RECORDS THAT CITE THIS RECORD
                               (9 CITINGS)
REFERENCE COUNT:         1     THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS
                               RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8   ANSWER 8 OF 10  CAPLUS  COPYRIGHT 2010 ACS on STN
ACCESSION NUMBER:        2000:880985  CAPLUS
DOCUMENT NUMBER:         134:37058
TITLE:                   Therapeutic use of an inhibitor of a hedgehog or a
                         hedgehog-related signaling pathway
INVENTOR(S):             Lamb, Jonathan Robert; Hoyne, Gerard Francis; Dallman,
                         Margaret Jane
PATENT ASSIGNEE(S):      Lorantis Limited, UK
SOURCE:                  PCT Int. Appl., 78 pp.
                         CODEN: PIXXD2
DOCUMENT TYPE:           Patent
LANGUAGE:                English
FAMILY ACC. NUM. COUNT:  1
PATENT INFORMATION:

     PATENT NO.          KIND   DATE        APPLICATION NO.        DATE
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     WO 2000074706        A1    20001214    WO 2000-GB2191         20000605 <--
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             DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ,
             CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG
     CA 2376210           A1    20001214    CA 2000-2376210        20000605 <--
     EP 1183040           A1    20020306    EP 2000-935413         20000605 <--
     EP 1183040           B1    20041201
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             IE, SI, LT, LV, FI, RO
     JP 2003501395        T     20030114    JP 2001-501240         20000605 <--
     AT 283700            T     20041215    AT 2000-935413         20000605 <--
     AU 780358            B2    20050317    AU 2000-50955          20000605 <--
     ES 2233383           T3    20050616    ES 2000-935413         20000605 <--
     US 20020192216       A1    20021219    US 2001-13310          20011207
PRIORITY APPLN. INFO.:                      GB 1999-13350       A  19990608
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                                            GB 1999-21953       A  19990916
                                            WO 2000-GB2191      W  20000605
ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT
AB   Use of an inhibitor of a Hedgehog signaling pathway, or an inhibitor of a
     pathway which is a target of the Hedgehog signaling pathway in the preparation
     of a medicament for treatment of epithelial cell hyperplasia, fibrosis of
     tissue, inflammation, cancer or an immune disorder.  Also a
     transgenic animal or cell line capable of expressing a component or an
     inhibitor of a hedgehog signaling pathway or a target pathway of the
     hedgehog signaling pathway.
OS.CITING REF COUNT:     9     THERE ARE 9 CAPLUS RECORDS THAT CITE THIS RECORD
                               (11 CITINGS)
REFERENCE COUNT:         8     THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS
                               RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8   ANSWER 9 OF 10  CAPLUS  COPYRIGHT 2010 ACS on STN
ACCESSION NUMBER:        2000:493313  CAPLUS
DOCUMENT NUMBER:         133:99549
TITLE:                   Regulation of the hedgehog pathway and smoothened
                         gain-of-function by gene patched agonists
INVENTOR(S):             Dudek, Henryk; Ji, Benxiu
PATENT ASSIGNEE(S):      Ontogeny, Inc., USA
SOURCE:                  PCT Int. Appl., 114 pp.
                         CODEN: PIXXD2
DOCUMENT TYPE:           Patent
LANGUAGE:                English
FAMILY ACC. NUM. COUNT:  1
PATENT INFORMATION:

     PATENT NO.          KIND   DATE        APPLICATION NO.        DATE
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     WO 2000041545        A2    20000720    WO 2000-US873          20000113 <--
     WO 2000041545        A3    20000928
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             IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA,
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     US 6291516           B1    20010918    US 1999-417564         19991014 <--
     CA 2370042           A1    20000720    CA 2000-2370042        20000113 <--
     EP 1143961           A2    20011017    EP 2000-906910         20000113 <--
         R:  AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
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     JP 2003517279        T     20030527    JP 2000-593166         20000113 <--
     AU 778866            B2    20041223    AU 2000-28491          20000113 <--
     US 20010034337       A1    20011025    US 2001-867311         20010529 <--
     US 6686388           B2    20040203
     US 20040127474       A1    20040701    US 2003-735116         20031212
     AU 2005201269        A1    20050421    AU 2005-201269         20050323
     AU 2005201269        B2    20080313
     US 20060020020       A1    20060126    US 2005-230063         20050919
PRIORITY APPLN. INFO.:                      US 1999-115642P     P  19990113
                                            US 1999-119594P     P  19990210
                                            US 1999-142124P     P  19990702
                                            US 1999-417564      A  19991014
                                            AU 2000-28491       A  20000113
                                            WO 2000-US873       W  20000113
                                            US 2001-867311      A1 20010529
                                            US 2003-735116      B1 20031212
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ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT
OTHER SOURCE(S):         MARPAT 133:99549
AB   The present invention makes available methods and reagents for inhibiting
     aberrant growth states resulting from hedgehog gain-of-function, patched
     (ptc) loss-of-function or smoothened gain-of-function comprising
     contacting a cell with a compound, such as a polypeptide or small mol. in an
     amount sufficient to control the aberrant growth state, e.g., to agonize a
     normal ptc pathway or antagonize smoothened or hedgehog activity.  The
     present invention further makes available methods and reagents for
     ameliorating the consequences of hedgehog loss-of-function, ptc
     gain-of-function, or smoothened loss-of-function comprising contacting a
     cell with a compound, such as a polypeptide or small mol., in an amount
     sufficient for amelioration.  In certain embodiments, the subject compds.,
     e.g., a cAMP analog, adenylate cyclase agonist, or cAMP phosphodiesterase
     inhibitor, regulate cAMP levels, which in turn modulates activity of the
     hedgehog pathway.  Thus, compds. such as jervine, cyclopamine, and
     forskolin analogs are also effective in inhibition of medulloblastoma.
OS.CITING REF COUNT:     11    THERE ARE 11 CAPLUS RECORDS THAT CITE THIS
                               RECORD (13 CITINGS)
REFERENCE COUNT:         8     THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS
                               RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8   ANSWER 10 OF 10  CAPLUS  COPYRIGHT 2010 ACS on STN
ACCESSION NUMBER:        1999:672583  CAPLUS
DOCUMENT NUMBER:         131:267077
TITLE:                   Use of steroidal alkaloid derivatives as inhibitors of
                         hedgehog signaling pathways
INVENTOR(S):             Beachy, Philip A.; Cooper, Michael K.; Porter, Jeffrey
                         A.
PATENT ASSIGNEE(S):      Johns Hopkins University School of Medicine, USA
SOURCE:                  PCT Int. Appl., 136 pp.
                         CODEN: PIXXD2
DOCUMENT TYPE:           Patent
LANGUAGE:                English
FAMILY ACC. NUM. COUNT:  1
PATENT INFORMATION:

     PATENT NO.          KIND   DATE       APPLICATION NO.       DATE
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     WO 9952534           A1    19991021   WO 1999-US7811        19990409 <--
         W:  AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE,
             DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP,
             KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN,
             MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM,
             TR, TT, UA, UG, US, UZ, VN, YU, ZW
         RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK,
             ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG,
             CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG
     US 20020006931       A1    20020117   US 1998-90622         19980604 <--
     US 6432970           B2    20020813
     CA 2326654           A1    19991021   CA 1999-2326654       19990409 <--
     AU 9934860           A     19991101   AU 1999-34860         19990409 <--
     AU 768130            B2    20031204
     EP 1067939           A1    20010117   EP 1999-916563        19990409 <--
         R:  AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
             IE, SI, LT, LV, FI, RO
     JP 2002511415        T     20020416   JP 2000-543144        19990409 <--
     IL 138645            A     20060820   IL 1999-138645        19990409 <--
     US 6867216           B1    20050315   US 2000-708974        20001108 <--
     US 7291626           B1    20071106   US 2000-708964        20001108 <--
     US 20060142245       A1    20060629   US 2005-270984        20051111
     US 20080058298       A1    20080306   US 2007-894712        20070820
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PRIORITY APPLN. INFO.:                      US 1998-81186P      P  19980409
                                            US 1998-81263P      P  19980409
                                            US 1998-90622       A  19980604
                                            WO 1999-US7811      W  19990409
                                            US 2000-685244      B1 20001010
                                            US 2000-708964      A3 20001108
ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT
OTHER SOURCE(S):         MARPAT 131:267077
AB   The present invention makes available assays and reagents inhibiting
     paracrine and/or autocrine signals produced by a hedgehog protein or
     aberrant activation of a hedgehog signal transduction pathway, e.g., which
     involve the use of a steroidal alkaloid or other small mol.
OS.CITING REF COUNT:     12    THERE ARE 12 CAPLUS RECORDS THAT CITE THIS
                               RECORD (13 CITINGS)
REFERENCE COUNT:         7     THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS
                               RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT


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                                                      ENTRY    SESSION
FULL ESTIMATED COST                                   52.56      58.77

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CA SUBSCRIBER PRICE                                  -10.20     -10.20

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                                                      ENTRY    SESSION
FULL ESTIMATED COST                                    3.33      62.10

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L9          SEL L1 1- CHEM :      31 TERMS

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CA SUBSCRIBER PRICE                                     0.00     -10.20

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S L1 OR L9


L11       7357 L1 OR L10

=> s l11 and (cancer or tumor or neoplasm)
L12       1644 L11 AND (CANCER OR TUMOR OR NEOPLASM)

=> s l12 and pd<20010702
L13        495 L12 AND PD<20010702

=> s l13 and apoptosis
L14         29 L13 AND APOPTOSIS

=> dup rem l14
PROCESSING COMPLETED FOR L14
L15          15 DUP REM L14 (14 DUPLICATES REMOVED)

=> d l15 1-15 ibib abs

L15  ANSWER 1 OF 15     MEDLINE on STN                   DUPLICATE 1
ACCESSION NUMBER:   2001506520     MEDLINE
DOCUMENT NUMBER:    PubMed ID: 11554450
TITLE:              SAG/ROC/Rbx/Hrt, a zinc RING finger gene family:
                    molecular cloning, biochemical properties, and biological
                    functions.
AUTHOR:             Sun Y; Tan M; Duan H; Swaroop M
CORPORATE SOURCE:   Cancer Molecular Sciences, Pfizer Global Research and
                    Development, Ann Arbor Laboratories, MI 48105, USA..
                    yi.sun@pfizer.com
SOURCE:             Antioxidants & redox signaling, (2001 Aug) Vol.
                    3, No. 4, pp. 635-50.  Ref: 106
                    Journal code: 100888899. ISSN: 1523-0864. L-ISSN:
                    1523-0864.
PUB. COUNTRY:       United States
DOCUMENT TYPE:      (COMPARATIVE STUDY)
                    Journal; Article; (JOURNAL ARTICLE)
                    General Review; (REVIEW)
LANGUAGE:           English
FILE SEGMENT:       Priority Journals
ENTRY MONTH:        200203
ENTRY DATE:         Entered STN: 17 Sep 2001
                    Last Updated on STN: 4 Mar 2003
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Entered Medline: 5 Mar 2002
REFERENCE COUNT: 106 There are 106 cited references for this document.

AB The RING (really interesting new gene) finger proteins containing a characteristic C3HC4 or C3H2C3 motif appear to act as E3 ubiquitin ligase and play important roles in many processes, including cell-cycle progression, oncogenesis, signal transduction, and development. This review is focused on SAG/ROC/Rbx/Hrt (sensitive to apoptosis gene/regulator of cullins/RING box protein), an evolutionarily conserved RING finger family of proteins that were cloned recently by several independent laboratories through differential display, yeast two-hybrid screening, or biochemical purification. SAG /ROC2/Rbx2/Hrt2 is expressed in multiple mouse adult tissues, as well as early embryos. In humans, both SAG and ROC1 are ubiquitously expressed at a very high level in heart, skeletal muscle, and testis. Expression of both SAG and ROC1 is induced by mitogenic stimulation. SAG is also induced by a redox agent in cultured cells, as well as in in vivo mouse brain upon ischemia/reperfusion. Structurally, SAG consists of four exons and three introns with at least one splicing variant and two pseudogenes. The SAG gene promoter is enriched with multiple transcription factor binding sites. Biochemically, SAG binds to RNA, has metal-ion binding/free radical scavenging activity, and is redox-sensitive. Most importantly, like ROC1, SAG/ROC2 binds to cullins and acts as an essential component of E3 ubiquitin ligase. Biologically, SAG is a growth-essential gene in yeast. In mammalian cells, SAG protects apoptosis mainly through inhibition of cytochrome c release/caspase activation, and promotes growth under serum deprivation at least in part by inhibiting p27 accumulation. Blocking SAG expression via antisense transfection inhibits tumor cell growth. Thus, SAG appears to be a valid drug target for anticancer therapy.

L15 ANSWER 2 OF 15 MEDLINE on STN
ACCESSION NUMBER: 2001565152 MEDLINE
DOCUMENT NUMBER: PubMed ID: 11668520
TITLE: Expression of the sensitive to apoptosis gene, SAG, as a prognostic marker in nonsmall cell lung cancer.
AUTHOR: Sasaki H; Yukiue H; Kobayashi Y; Moriyama S; Nakashima Y; Kaji M; Fukai I; Kiriyama M; Yamakawa Y; Fujii Y
CORPORATE SOURCE: Department of Surgery II, Nagoya City University Medical School, Nagoya, Japan.. hisasaki@med.nagoya-cu.ac.jp
SOURCE: International journal of cancer. Journal international du cancer, (2001 Nov 20) Vol. 95, No. 6, pp. 375-7.
Journal code: 0042124. ISSN: 0020-7136. L-ISSN: 0020-7136.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200112
ENTRY DATE: Entered STN: 23 Oct 2001
Last Updated on STN: 2 Jan 2003
Entered Medline: 4 Dec 2001

AB Inhibition of programmed cell death (apoptosis) is associated with increased tumor aggressiveness. We hypothesized that a novel sensitive to apoptosis gene, SAG, may be expressed in tumors of patients with nonsmall cell lung cancer (NSCLC) and may affect their clinical outcome. Expression of SAG messenger RNA was evaluated by reverse transcription polymerase chain reaction in 80 nonsmall cell lung carcinomas and 65 adjacent histologic nonmalignant lung samples using a LightCycler. The data were analyzed in reference to clinicopathologic data and survival.

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     The SAG/GAPDH mRNA level in 80 NSCLC was 2.337 +/- 1.972.  Of 65
     paired NSCLC and nonmalignant lung samples, SAG/GAPDH mRNA
     levels were 2.313 +/- 2.064 and 1.696 +/- 1.910, respectively.  The
     SAG mRNA level was significantly higher in NSCLC compared with
     nonmalignant lung tissue (p = 0.0169).  There was no relationship between
     SAG gene expression and age, gender, T- or N-status or clinical
     stages.  The NSCLC patients with high SAG/GAPDH expression
     (>1.8) had significantly poorer survival than the patients with low
     SAG/GAPDH expression (<1.8, p = 0.0227).  Thus we suggest that
     SAG gene expression in NSCLC may be a useful prognostic marker.
     Copyright 2001 Wiley-Liss, Inc.

L15  ANSWER 3 OF 15     MEDLINE on STN                  DUPLICATE 2
ACCESSION NUMBER:   2001473536     MEDLINE
DOCUMENT NUMBER:    PubMed ID: 11306146
TITLE:              Differential clonal expansion of CD4 and CD8 T cells in
                    response to 4-1BB ligation: contribution of 4-1BB during
                    inflammatory responses.
AUTHOR:             Takahashi C; Mittler R S; Vella A T
CORPORATE SOURCE:   Department of Microbiology, 220 Nash Hall, Oregon State
                    University, Corvallis, OR 97331, USA.
CONTRACT NUMBER:    AI42858A (United States NIAID NIH HHS)
SOURCE:             Immunology letters, (2001 Apr 2) Vol. 76, No. 3,
                    pp. 183-91.
                    Journal code: 7910006. ISSN: 0165-2478. L-ISSN: 0165-2478.
PUB. COUNTRY:       Netherlands
DOCUMENT TYPE:      Journal; Article; (JOURNAL ARTICLE)
                    (RESEARCH SUPPORT, U.S. GOV'T, P.H.S.)
LANGUAGE:           English
FILE SEGMENT:       Priority Journals
ENTRY MONTH:        200108
ENTRY DATE:         Entered STN: 27 Aug 2001
                    Last Updated on STN: 27 Aug 2001
                    Entered Medline: 23 Aug 2001
AB   Cell surface proteins of the tumor necrosis factor (TNF) family
     of receptors have been intimately involved in inducing T cell death.  A
     feature of these family members that is less well studied is their ability
     to rescue T cells from apoptosis.  One such member is 4-1BB; an
     activation induced surface receptor on CD4 and CD8 T cells.  This study
     demonstrates that the costimulatory effects of 4-1BB, which was found to
     enhance clonal expansion, required cross-linking of the receptor.  The
     survival of the activated CD8 T cells following expansion was not
     associated with an increase in Bcl-2 expression.  Provided that 4-1BB
     signaling was present, the amplification of activated CD8 T cell growth in
     vivo was independent of CD28 ligation.  In vivo clonal expansion of
     activated CD4 T cells, however, was not as responsive to 4-1BB
     cross-linking.  Moreover, 4-1BB-induced expansion was comparable to that
     mediated by LPS which can incite multiple costimulatory signals.
     Furthermore, LPS-mediated growth and survival of superantigen (SAg
     ) stimulated T cells appeared to be partially dependent on interactions
     between 4-1BB and 4-1BB ligand (4-1BBL).

L15  ANSWER 4 OF 15     MEDLINE on STN                  DUPLICATE 3
ACCESSION NUMBER:   2001194526     MEDLINE
DOCUMENT NUMBER:    PubMed ID: 11255265
TITLE:              Elevated expression of SAG/ROC2/Rbx2/Hrt2 in
                    human colon carcinomas: SAG does not induce
                    neoplastic transformation, but antisense SAG
                    transfection inhibits tumor cell growth.
AUTHOR:             Huang Y; Duan H; Sun Y
CORPORATE SOURCE:   Department of Molecular Biology, Pfizer Global Research and
                    Development, Ann Arbor Laboratories, Ann Arbor, Michigan
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                        48105, USA.
SOURCE:                 Molecular carcinogenesis, (2001 Jan) Vol. 30, No.
                        1, pp. 62-70.
                        Journal code: 8811105. ISSN: 0899-1987. L-ISSN: 0899-1987.
PUB. COUNTRY:           United States
DOCUMENT TYPE:          Journal; Article; (JOURNAL ARTICLE)
LANGUAGE:               English
FILE SEGMENT:           Priority Journals
ENTRY MONTH:            200104
ENTRY DATE:             Entered STN: 10 Apr 2001
                        Last Updated on STN: 10 Apr 2001
                        Entered Medline: 5 Apr 2001
AB   Sensitive-to-apoptosis gene (SAG)/regulator of cullins
     (ROC)2/Rbx2/Hrt2 is a newly identified component of SCF E3 ubiquitin
     ligase that controls cell-cycle progression by promoting ubiquitination
     and degradation of cell-cycle inhibitors.  We recently found that
     SAG protects cells from apoptosis induced by redox
     agents, promotes S-phase entry and cell growth under serum starvation, and
     is required for yeast growth.  In the present study, we report that the
     SAG protein level was elevated in six of 10 human colon carcinoma
     tissues (60%) as compared with adjacent normal tissues from the same
     patient.  SAG overexpression in preneoplastic cells in a JB6
     tumor promotion-and-progression model did not induce neoplastic
     transformation, and SAG overexpression in NIH/3T3 cells did not
     induce transforming foci formation, suggesting that SAG is not a
     dominant oncogene.  However, when DLD-1 human colon carcinoma cells were
     transfected with antisense SAG, monolayer growth was
     significantly inhibited, as shown by a decreased number of stable colonies
     in the plate after normalization with transfection efficiency.  Stable
     clones that expressed antisense SAG showed a 50% decrease in
     their ability to form colonies when grown in soft agar versus clones that
     did not express antisense SAG.  We found an inverse correlation
     in four of 10 tumors between the levels of SAG and
     p27, a cyclin-dependent kinase inhibitor.  We concluded that SAG
     is not causally related to cellular transformation, but its overexpression
     may be important for the maintenance of tumor cell phenotype.
     Therefore, targeting SAG expression may have therapeutic value
     in cancer treatment.  Mol.  Carcinog. 30:62-70, 2001.
     Copyright 2001 Wiley-Liss, Inc.

L15  ANSWER 5 OF 15     MEDLINE on STN                    DUPLICATE 4
ACCESSION NUMBER:       2001194523     MEDLINE
DOCUMENT NUMBER:        PubMed ID: 11255262
TITLE:                  Promotion of S-phase entry and cell growth under serum
                        starvation by SAG/ROC2/Rbx2/Hrt2, an E3 ubiquitin
                        ligase component: association with inhibition of p27
                        accumulation.
AUTHOR:                 Duan H; Tsvetkov L M; Liu Y; Song Y; Swaroop M; Wen R; Kung
                        H F; Zhang H; Sun Y
CORPORATE SOURCE:       Department of Molecular Biology, Pfizer Global Research and
                        Development, Ann Arbor Laboratories, Ann Arbor, Michigan
                        48105, USA.
SOURCE:                 Molecular carcinogenesis, (2001 Jan) Vol. 30, No.
                        1, pp. 37-46.
                        Journal code: 8811105. ISSN: 0899-1987. L-ISSN: 0899-1987.
PUB. COUNTRY:           United States
DOCUMENT TYPE:          Journal; Article; (JOURNAL ARTICLE)
LANGUAGE:               English
FILE SEGMENT:           Priority Journals
ENTRY MONTH:            200104
ENTRY DATE:             Entered STN: 10 Apr 2001
                        Last Updated on STN: 4 Mar 2003
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                    Entered Medline: 5 Apr 2001
AB   The sensitive-to-apoptosis gene (SAG) was initially
     identified as a redox-inducible, apoptosis-protective protein
     and subsequently found to be the second family member of regulator of
     cullins (ROC)/RING box protein (Rbx)/Hrt, which acts as a component of E3
     ubiquitin ligase.  We report here that SAG promoted cell growth
     under serum starvation.  Microinjection of SAG mRNA into
     quiescent NIH/3T3 cells induced S-phase entry as determined by
     [(3)H]-thymidine incorporation.  Likewise, overexpression of SAG
     by either adenovirus infection of immortalized human epidermal
     keratinocytes (Rhek-1) or DNA transfection of SY5Y human neuroblastoma
     cells induced cell proliferation under serum starvation.  Because
     cyclin-dependent kinase inhibitors (CKIs), including p21, p27, and p57,
     are degraded through the ubiquitin pathway, we tested whether SAG
     -induced cell growth is associated with CKI degradation.  Although there
     was no significant difference in the levels of p21 and p57 between the
     vector controls and SAG-overexpressing cells, serum starvation
     induced 10- to 18-fold accumulation of p27 in control Rhek-1 cells.
     Accumulation of p27 was remarkably inhibited (only 2 to 5-fold) in
     SAG-infected cells.  Inhibition of p27 accumulation was also
     observed in stably SAG-overexpressing SY5Y cells.
     Significantly, SAG-associated inhibition of p27 accumulation was
     largely abolished by the treatment with a proteasome inhibitor.  In vivo
     binding of SAG and Skp2, an F-box protein that promotes p27
     ubiquitination, was detected, and the binding was enhanced in SAG
     -overexpressing cells grown under serum starvation.  Thus, SAG
     -induced growth with serum withdrawal appears to be associated with
     SAG-mediated p27 degradation.  Mol.  Carcinog. 30:37-46, 2001.
     Copyright 2001 Wiley-Liss, Inc.

L15  ANSWER 6 OF 15     MEDLINE on STN                  DUPLICATE 5
ACCESSION NUMBER:   2000450267     MEDLINE
DOCUMENT NUMBER:    PubMed ID: 11005251
TITLE:              Identification and characterization of genes responsive to
                    apoptosis: application of DNA chip technology and
                    mRNA differential display.
AUTHOR:             Sun Y
CORPORATE SOURCE:   Department of Molecular Biology, Pfizer Global Research and
                    Development, Ann Arbor, MI 48105, USA.. yi.sun@wl.com
SOURCE:             Histology and histopathology, (2000 Oct) Vol. 15,
                    No. 4, pp. 1271-84.  Ref: 135
                    Journal code: 8609357. ISSN: 0213-3911. L-ISSN: 0213-3911.
PUB. COUNTRY:       Spain
DOCUMENT TYPE:      Journal; Article; (JOURNAL ARTICLE)
                    General Review; (REVIEW)
LANGUAGE:           English
FILE SEGMENT:       Priority Journals
ENTRY MONTH:        200102
ENTRY DATE:         Entered STN: 22 Mar 2001
                    Last Updated on STN: 22 Mar 2001
                    Entered Medline: 2 Feb 2001
REFERENCE COUNT:    135  There are 135 cited references for this document.
AB   Apoptosis (programmed cell death) is a genetically programmed
     active cell death process for maintaining homeostasis under physiological
     conditions and for responding to various stimuli.  Many human diseases
     have been associated with either increased apoptosis (such as
     AIDS and neurodegenerative disorders) or decreased apoptosis
     (such as cancer and autoimmune disorders).  In an attempt to
     understand apoptosis signaling pathway and genes associated with
     apoptosis, we established two cell model systems on which
     apoptosis is induced either by DNA damaging agent, etoposide or by
     redox agent, 1,10-phenanthroline (OP).  DNA chip profiling or mRNA
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differential display (DD) was utilized to identify genes responsive to apoptosis induced by these two agents. In etoposide model with chip hybridization, we defined signaling pathways that mediate apoptosis in p53 dependent manner (through activation of p53 target genes such as Waf-1/p21, PCNA, GPX, S100A2 and PTGF-beta) as well as in p53-independent manner (through activation of ODC and TGF-beta receptor, among others). In OP model with DD screening, we cloned and characterized two genes: glutathione synthetase, encoding an enzyme involved in glutathione synthesis and Sensitive to Apoptosis Gene (SAG), a novel evolutionarily conserved gene encoding a zinc RING finger protein. Both genes appear to protect cells from apoptosis induced by redox agents. Further characterization of SAG revealed that it is a growth essential gene in yeast and belongs to a newly identified gene family that promotes protein ubiquitination and degradation. Through this activity, SAG regulates cell cycle progression and many other key biological processes. Thus, SAG could be a valid drug target for anti-cancer and anti-inflammation therapies.

L15 ANSWER 7 OF 15 MEDLINE on STN
ACCESSION NUMBER: 2000463765 MEDLINE
DOCUMENT NUMBER: PubMed ID: 11016595
TITLE: Alleviation of renal disease and lymphadenopathy in MRL-Fasp(lrcg)/Fas(lprcg) (MR-lpr(cg)) mice neonatally infected with mouse mammary tumor virus encoding superantigen strongly reactive with TCR Vbeta8.2 element.
AUTHOR: Matsuzawa A; Yasuda T; Zhang Y; Nagase H; Yoshimoto T; Kimura M; Tsubura A
CORPORATE SOURCE: Laboratory Animal Research Center, Institute of Medical Science, University of Tokyo, Japan.. atmatsu@oregano.ocn.ne.jp
SOURCE: Viral immunology, (2000) Vol. 13, No. 3, pp. 297-311.
Journal code: 8801552. ISSN: 0882-8245. L-ISSN: 0882-8245.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
(RESEARCH SUPPORT, NON-U.S. GOV'T)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200102
ENTRY DATE: Entered STN: 22 Mar 2001
Last Updated on STN: 22 Mar 2001
Entered Medline: 15 Feb 2001

AB Mouse mammary tumor virus transmitted by FM mice (FM-MMTV) encodes a superantigen (SAg) characterized by strong reactivity with TCR Vbeta8.2 element and broad spectrum of Vbeta reactivity. To investigate what effects the expression in vivo of FM-MMTV SAg exhibits on the course of the disease in a lupus-prone model, MRL/MpJ-Fas(lprcg)/Fas(lprcg) (MRL-lpr9cg) mice, neonatally FM-MMTV-infected MRL-lprcg(MMTV) and uninfected MRL-lpr(cg) mice were compared for various disease parameters. In MRL-lprcg(MMTV), survival was significantly prolonged, glomerulonephritis, proteinuria, and lymphadenopathy were clearly ameliorated, and the production of serum immunoglobulin G (IgG), complement-activating IgG2a, and cryogenic IgG3 autoantibodies, which are thought to be pathogenic to kidneys, and circulating immune complexes (IC), and glomerular IC deposition were significantly suppressed. FM-MMTV infection deleted Vbeta8.2+ cells by about 90% and Vbeta14+ cells less efficiently in all of the CD4+, CD8+, and B220+ CD4- CD8- or double-negative (DN) T-cell populations, and Vbeta8.1+ cells in the CD4+ population but not in the others. Similar deletion profiles of CD8+ and DN T cells support that DN T cells are derived from the CD8 lineage. The results imply that the specific

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     regulation of the immune system with viral SAg has a potential
     for development of an attractive immunomodulatory therapy of autoimmune
     diseases.

L15  ANSWER 8 OF 15     MEDLINE on STN
ACCESSION NUMBER:   1999182502     MEDLINE
DOCUMENT NUMBER:    PubMed ID: 10082581
TITLE:              SAG, a novel zinc RING finger protein that
                    protects cells from apoptosis induced by redox
                    agents.
AUTHOR:             Duan H; Wang Y; Aviram M; Swaroop M; Loo J A; Bian J; Tian
                    Y; Mueller T; Bisgaier C L; Sun Y
CORPORATE SOURCE:   Departments of Molecular Biology, Parke-Davis
                    Pharmaceutical Research, Division of Warner-Lambert
                    Company, Ann Arbor, Michigan 48105, USA.
SOURCE:             Molecular and cellular biology, (1999 Apr) Vol.
                    19, No. 4, pp. 3145-55.
                    Journal code: 8109087. ISSN: 0270-7306. L-ISSN: 0270-7306.
                    Report No.: NLM-PMC84108.
PUB. COUNTRY:       United States
DOCUMENT TYPE:      (COMPARATIVE STUDY)
                    Journal; Article; (JOURNAL ARTICLE)
LANGUAGE:           English
FILE SEGMENT:       Priority Journals
OTHER SOURCE:       GENBANK-AF092877; GENBANK-AF092878
ENTRY MONTH:        199904
ENTRY DATE:         Entered STN: 4 May 1999
                    Last Updated on STN: 2 Jan 2003
                    Entered Medline: 20 Apr 1999
MEDLINE REFERENCE COUNT:   72    There are 72 cited references available in
                                 MEDLINE for this document.
AB   SAG (sensitive to apoptosis gene) was cloned as an
     inducible gene by 1,10-phenanthroline (OP), a redox-sensitive compound and
     an apoptosis inducer.  SAG encodes a novel zinc RING
     finger protein that consists of 113 amino acids with a calculated
     molecular mass of 12.6 kDa.  SAG is highly conserved during
     evolution, with identities of 70% between human and Caenorhabditis elegans
     sequences and 55% between human and yeast sequences.  In human tissues,
     SAG is ubiquitously expressed at high levels in skeletal muscles,
     heart, and testis.  SAG is localized in both the cytoplasm and
     the nucleus of cells, and its gene was mapped to chromosome 3q22-24.
     Bacterially expressed and purified human SAG binds to zinc and
     copper metal ions and prevents lipid peroxidation induced by copper or a
     free radical generator.  When overexpressed in several human cell lines,
     SAG protects cells from apoptosis induced by redox
     agents (the metal chelator OP and zinc or copper metal ions).
     Mechanistically, SAG appears to inhibit and/or delay metal
     ion-induced cytochrome c release and caspase activation.  Thus,
     SAG is a cellular protective molecule that appears to act as an
     antioxidant to inhibit apoptosis induced by metal ions and
     reactive oxygen species.

L15  ANSWER 9 OF 15     MEDLINE on STN                   DUPLICATE 6
ACCESSION NUMBER:   1999435944     MEDLINE
DOCUMENT NUMBER:    PubMed ID: 10506102
TITLE:              Alterations of SAG mRNA in human cancer
                    cell lines: requirement for the RING finger domain for
                    apoptosis protection.
AUTHOR:             Sun Y
CORPORATE SOURCE:   Department of Molecular Biology, Parke-Davis Pharmaceutical
                    Research, Division of Warner-Lambert Co., Ann Arbor, MI
                    48105, USA.. yi.sun@wl.com
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SOURCE:              Carcinogenesis, (1999 Oct) Vol. 20, No. 10, pp.
                     1899-903.
                     Journal code: 8008055. ISSN: 0143-3334. L-ISSN: 0143-3334.
PUB. COUNTRY:        ENGLAND: United Kingdom
DOCUMENT TYPE:       Journal; Article; (JOURNAL ARTICLE)
LANGUAGE:            English
FILE SEGMENT:        Priority Journals
ENTRY MONTH:         199911
ENTRY DATE:          Entered STN: 11 Jan 2000
                     Last Updated on STN: 2 Jan 2003
                     Entered Medline: 4 Nov 1999
AB   We have recently cloned and characterized a novel zinc RING finger gene,
     SAG (sensitive to apoptosis gene).  SAG has
     antioxidant activity and protects cells from apoptosis induced
     by metal ions and redox compounds.  During the course of SAG
     cloning, we identified two forms of deletions of SAG mRNA in
     colon and testicular carcinoma cell lines.  The first form (SAG
     -MU1) consists of a 7 bp deletion that results in a frameshift and
     abolishes the RING finger domain.  The second (SAG-MU2) consists
     of an in-frame 48 bp deletion that truncates 16 amino acids in the protein
     but retains the RING finger domain.  Functional studies using stable
     transfectant lines reveal that, like wild-type SAG, SAG
     -MU2 retains anti-apoptosis activity, whereas SAG-MU1
     shows no such protection.  The results indicate that the C-terminal zinc
     RING finger domain is required for anti-apoptosis activity of
     SAG.

L15  ANSWER 10 OF 15     MEDLINE on STN                DUPLICATE 7
ACCESSION NUMBER:    1999236838     MEDLINE
DOCUMENT NUMBER:     PubMed ID: 10221649
TITLE:               In vivo elimination of viral superantigen-activated CD4+ T
                     cells: apoptosis occurs at a distance from the
                     activation site.
AUTHOR:              Le Bon A; Wache A C; Papiernik M
CORPORATE SOURCE:    INSERM U345, Institut Necker, Paris, France.
SOURCE:              International immunology, (1999 Mar) Vol. 11, No.
                     3, pp. 373-82.
                     Journal code: 8916182. ISSN: 0953-8178. L-ISSN: 0953-8178.
PUB. COUNTRY:        ENGLAND: United Kingdom
DOCUMENT TYPE:       (COMPARATIVE STUDY)
                     Journal; Article; (JOURNAL ARTICLE)
                     (RESEARCH SUPPORT, NON-U.S. GOV'T)
LANGUAGE:            English
FILE SEGMENT:        Priority Journals
ENTRY MONTH:         199906
ENTRY DATE:          Entered STN: 14 Jul 1999
                     Last Updated on STN: 14 Jul 1999
                     Entered Medline: 29 Jun 1999
AB   Local injection of mouse mammary tumor virus (MMTV) induces a
     local immune response, with activation of viral superantigen
     (vSAG)-specific T cell subsets followed by their clonal deletion.  We
     investigated the fate of vSAG-reactive T cells following footpad injection
     of MMTV(SW) to mice.  Activated T cells accumulated in draining lymph
     nodes.  However, we demonstrated that apoptosis did not occur at
     the activation site, on the contrary of what has been shown after
     bacterial SAG activation.  Although activated T cells were
     already shown to have the capacity to migrate to the gut, the fate of gut
     homing cells remains unclear.  We demonstrate that the number of
     vSAG-specific T cells activated in the periphery was increasing in the
     follicles of gut-associated lymphoid organs, together with the number of
     apoptotic cell clusters.  These results strongly suggested that
     gut-associated lymphoid tissue was the specific graveyard for apoptotic
     vSAG-activated CD4 T cells.

L15  ANSWER 11 OF 15     MEDLINE on STN
ACCESSION NUMBER:   1998261452     MEDLINE
DOCUMENT NUMBER:    PubMed ID: 9596673
TITLE:              Viral superantigen-induced negative selection of TCR
                    transgenic CD4+ CD8+ thymocytes depends on activation, but
                    not proliferation.
AUTHOR:             Ferrero I; Anjuere F; Azcoitia I; Renno T; MacDonald H R;
                    Ardavin C
CORPORATE SOURCE:   Department of Cell Biology, Faculty of Biology, Complutense
                    University, Madrid, Spain.
SOURCE:             Blood, (1998 Jun 1) Vol. 91, No. 11, pp. 4248-54.
                    Journal code: 7603509. ISSN: 0006-4971. L-ISSN: 0006-4971.
PUB. COUNTRY:       United States
DOCUMENT TYPE:      Journal; Article; (JOURNAL ARTICLE)
                    (RESEARCH SUPPORT, NON-U.S. GOV'T)
LANGUAGE:           English
FILE SEGMENT:       Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH:        199806
ENTRY DATE:         Entered STN: 13 Jul 1998
                    Last Updated on STN: 13 Jul 1998
                    Entered Medline: 26 Jun 1998
AB   T-cell negative selection, a process by which intrathymic immunological
     tolerance is induced, involves the apoptosis-mediated clonal
     deletion of potentially autoreactive T cells.  Although different
     experimental approaches suggest that this process is triggered as the
     result of activation-mediated cell death, the signal transduction pathways
     underlying this process is not fully understood.  In the present report we
     have used an in vitro system to analyze the cell activation and
     proliferation requirements for the deletion of viral superantigen (
     SAg)-reactive Vbeta8.1 T-cell receptor (TCR) transgenic (TG)
     thymocytes.  Our results indicate that in vitro negative selection of
     viral SAg-reactive CD4+ CD8+ thymocytes is dependent on
     thymocyte activation but does not require the proliferation of the
     negatively signaled thymocytes.

L15  ANSWER 12 OF 15     MEDLINE on STN
ACCESSION NUMBER:   1996228286     MEDLINE
DOCUMENT NUMBER:    PubMed ID: 8640876
TITLE:              Deletion of peripheral V beta 14+ T cells by Mtv-2-encoded
                    viral superantigen preceded by blastogenesis and DNA
                    synthesis but not by specific expansion.
AUTHOR:             Nakano H; Yoshimoto T; Nariuchi H; Kakiuchi T; Matsuzawa A
CORPORATE SOURCE:   Laboratory Animal Research Center, Institute of Medical
                    Science, University of Tokyo, Japan.
SOURCE:             Cellular immunology, (1996 Mar 15) Vol. 168, No.
                    2, pp. 281-90.
                    Journal code: 1246405. ISSN: 0008-8749. L-ISSN: 0008-8749.
PUB. COUNTRY:       United States
DOCUMENT TYPE:      (COMPARATIVE STUDY)
                    Journal; Article; (JOURNAL ARTICLE)
                    (RESEARCH SUPPORT, NON-U.S. GOV'T)
LANGUAGE:           English
FILE SEGMENT:       Priority Journals
ENTRY MONTH:        199607
ENTRY DATE:         Entered STN: 26 Jul 1996
                    Last Updated on STN: 3 Feb 1997
                    Entered Medline: 17 Jul 1996
AB   Exogenous and endogenous mouse mammary tumor viruses encode
     superantigen (SAG) in the 3' long terminal repeat.  We
     investigated the immune response of lymph node cells to the viral
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SAG encoded by endogenous Mtv-2 (vSAG-2) by i.v. injecting splenocytes from Mtv-2+ mice into Mtv-2- congenic counterparts. vSAG-2 stimulation induced blastogenesis and DNA synthesis but not subsequent specific expansion of V beta 14+CD4+ or CD8+ T lymphocytes. Instead, immediate deletion of these T cells progressed after vSAG-2 stimulation, and it was more prominent in both rapidity and degree in CD4+ than CD8+ population and in I-E+ than I-E- mice. vSAG-7 stimulation caused specific expansion of V beta 6+ T cells prior to their deletion as reported. vSAG-7 but not vSAG-2 induced IL-2R expression in the specific T cells. Moreover, the percentage of 5-bromo-2'-deoxyuridine-incorporated cells was about twofold higher in Vbeta6+ T cells stimulated with vSAG-7 than in V beta 14+ T cells stimulated with vSAG-2. The results suggest that vSAG-2 may be a weak mitogen against specific T cells and that T cells weakly activated by SAG may die without preceding expansion. In addition, proliferation of lymphocytes, especially B cells, and enhancement of the expression of IL-2, IL-4, and IFN-gamma messenger RNA were observed. Thus, V beta 14+ T cells stimulated with vSAG-2 were activated to produce cytokines and depleted quickly.

L15 ANSWER 13 OF 15 MEDLINE on STN
ACCESSION NUMBER: 1996042152 MEDLINE
DOCUMENT NUMBER: PubMed ID: 7595225
TITLE: CD40 ligation induces Apo-1/Fas expression on human B lymphocytes and facilitates apoptosis through the Apo-1/Fas pathway.
AUTHOR: Schattner E J; Elkon K B; Yoo D H; Tumang J; Krammer P H; Crow M K; Friedman S M
CORPORATE SOURCE: Department of Medicine, Hospital for Special Surgery, New York 10021, USA.
CONTRACT NUMBER: AI32634 (United States NIAID NIH HHS)
P50AR 42588 (United States NIAMS NIH HHS)
SOURCE: The Journal of experimental medicine, (1995 Nov 1)
Vol. 182, No. 5, pp. 1557-65.
Journal code: 2985109R. ISSN: 0022-1007. L-ISSN: 0022-1007.
Report No.: NLM-PMC2192191.
PUB. COUNTRY: United States
DOCUMENT TYPE: (COMPARATIVE STUDY)
Journal; Article; (JOURNAL ARTICLE)
(RESEARCH SUPPORT, NON-U.S. GOV'T)
(RESEARCH SUPPORT, U.S. GOV'T, P.H.S.)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199512
ENTRY DATE: Entered STN: 24 Jan 1996
Last Updated on STN: 6 Feb 1998
Entered Medline: 4 Dec 1995
MEDLINE REFERENCE COUNT: 44 There are 44 cited references available in MEDLINE for this document.

AB The Apo-1/Fas antigen (CD95) mediates programmed cell death of lymphocytes when bound by Fas ligand or anti-Apo-1/Fas antibody. In contrast, the CD40 antigen provides a potent activation and survival signal to B lymphocytes when it is engaged by its T cell ligand (CD40L, gp39) or cross-linked by anti-CD40 antibody. In this study, we use human tonsillar B cells and the Ramos Burkitt's lymphoma B cell line, which serves as a model for human germinal center B lymphocytes, to study the effectors of Apo-1/Fas expression and apoptosis of human B cells. We found that Apo-1/Fas expression was upregulated on both malignant and normal human B lymphocytes after CD40 ligation induced by (a) cognate T helper-B cell interaction mediated by microbial superantigen (SAg); (b) contact-dependent interaction with CD40L+, but not CD40L- Jurkat mutant T cell clones; and (c) monoclonal anti-CD40, but not any of a panel of control antibodies. Enhanced B cell Fas/Apo-1 expression is functionally

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     significant.  Coculture of Ramos Burkitt's lymphoma line cells with
     irradiated SAg-reactive CD4+ T cells with SAg or
     CD40L+ Jurkat T cells results in B cell apoptosis, evidenced by
     reduced cell viability and DNA laddering.  This process is augmented by
     the addition of anti-Apo-1/Fas monoclonal antibody, consistent with an
     acquired susceptibility to Apo-1/Fas-mediated apoptosis.  These
     data support an immunoregulatory pathway in which seemingly contradictory
     signals involving the B cell proliferation/survival antigen CD40, as well
     as the Apo-1/Fas molecule, which mediates programmed cell death of
     lymphocytes, are linked in the process of human B cell activation.

L15  ANSWER 14 OF 15     MEDLINE on STN                 DUPLICATE 8
ACCESSION NUMBER:    1995176373     MEDLINE
DOCUMENT NUMBER:     PubMed ID: 7871569
TITLE:               Differential effects of the immunosuppressive agents
                     cyclosporine and leflunomide in vivo. Leflunomide blocks
                     clonal T cell expansion yet allows production of
                     lymphokines and manifestation of T cell-mediated shock.
AUTHOR:              Lang R; Wagner H; Heeg K
CORPORATE SOURCE:    Institute of Medical Microbiology and Hygiene, Technical
                     University of Munich, Germany.
SOURCE:              Transplantation, (1995 Feb 15) Vol. 59, No. 3,
                     pp. 382-9.
                     Journal code: 0132144. ISSN: 0041-1337. L-ISSN: 0041-1337.
PUB. COUNTRY:        United States
DOCUMENT TYPE:       (COMPARATIVE STUDY)
                     Journal; Article; (JOURNAL ARTICLE)
                     (RESEARCH SUPPORT, NON-U.S. GOV'T)
LANGUAGE:            English
FILE SEGMENT:        Priority Journals
ENTRY MONTH:         199503
ENTRY DATE:          Entered STN: 7 Apr 1995
                     Last Updated on STN: 7 Apr 1995
                     Entered Medline: 30 Mar 1995
AB   The effects of leflunomide and CsA on immune responses in vitro and in
     vivo were investigated.  Like CsA, leflunomide inhibited mitogen- or
     antigen-driven T cell proliferation in vitro.  However, leflunomide
     impaired neither the capability of T cells to produce IL-2 and IL-4, nor
     the expression of IL-2R, that is, the acquisition of competence.  In
     contrast to CsA, the IL-2-driven growth of secondary T cells was blocked
     by leflunomide.  Cell cycle analyses revealed that activated T cells did
     not enter S phase of the cell cycle in the presence of leflunomide.  Next,
     the effects of leflunomide and CsA on the T cell response toward the
     bacterial superantigen (SAg) staphylococcal enterotoxin B (SEB)
     were analyzed in vivo.  SEB-induced early deletion (apoptosis)
     of a fraction of SEB-reactive V beta 8+ T cells and IL-2R expression were
     not impaired by either CsA nor leflunomide.  On the other hand, both CsA
     and leflunomide prevented V beta 8-selective clonal T cell expansion and
     generation of SEB-specific cytolytic activity.  In contrast to CsA,
     leflunomide treatment permitted in vivo SEB-induced production of T
     cell-derived lymphokines (IL-2 and TNF).  Further, leflunomide failed to
     protect D-galactosamine-sensitized mice from SEB-induced, T cell-mediated
     lethal shock, whereas CsA was fully protective.  Manifestation of
     SEB-induced T cell anergy was not impaired by leflunomide.  Our results
     provide evidence that CsA and leflunomide differ significantly in their
     functional properties to suppress immune responses in that both agents
     inhibit T cell functions linked to clonal expansion, while leflunomide
     does not inhibit lymphokine secretion and thus permits lymphokine-mediated
     immune functions.

L15  ANSWER 15 OF 15     MEDLINE on STN                 DUPLICATE 9
ACCESSION NUMBER:    1993314692     MEDLINE
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DOCUMENT NUMBER:    PubMed ID: 8100773
TITLE:              Activation with superantigens induces programmed death in
                    antigen-primed CD4+ class II+ major histocompatibility
                    complex T lymphocytes via a CD11a/CD18-dependent mechanism.
AUTHOR:             Damle N K; Leytze G; Klussman K; Ledbetter J A
CORPORATE SOURCE:   Bristol-Myers Squibb Pharmaceutical Research Institute,
                    Seattle.
SOURCE:             European journal of immunology, (1993 Jul) Vol.
                    23, No. 7, pp. 1513-22.
                    Journal code: 1273201. ISSN: 0014-2980. L-ISSN: 0014-2980.
PUB. COUNTRY:       GERMANY: Germany, Federal Republic of
DOCUMENT TYPE:      (IN VITRO)
                    Journal; Article; (JOURNAL ARTICLE)
LANGUAGE:           English
FILE SEGMENT:       Priority Journals
ENTRY MONTH:        199308
ENTRY DATE:         Entered STN: 20 Aug 1993
                    Last Updated on STN: 6 Feb 1995
                    Entered Medline: 9 Aug 1993
AB   Staphylococcal enterotoxin superantigens (SAg) bind class II
     major histocompatibility complex (MHC) molecules on antigen-presenting
     cells (APC) and upon cell-to-cell contact stimulate proliferation of T
     cells expressing appropriate V beta gene products.  In addition,
     SAg can also deliver negative signals to Ag-specific T cells
     resulting in a state of unresponsiveness or a loss of viability.  The
     present study examines the functional consequences of a direct interaction
     of SAg with alloAg-specific class II MHC+ CD4+ T cell lines
     (TCL).  Our results demonstrate that SAg induce programmed death
     (apoptosis) in a majority of Ag-specific CD4+ T cells
     accompanied by genomic DNA fragmentation.  SAg binding to
     Ag-specific TCL resulted in a rapid mobilization of intracellular free
     calcium ([Ca2+]i) and transcription of a number of cytokine genes
     including interleukin-2(IL-2), IL-4, interferon-gamma (IFN-gamma),
     granulocyte-macrophage colony-stimulating factor (GM-CSF), and granzyme B
     indicating the activation of primed T cells.  Both SAg-induced
     cytokine gene expression as well as subsequent death were significantly
     inhibited by a tyrosine kinase inhibitor herbimycin A and also by
     cyclosporin A.  SAg-induced death of primed T cells was also
     inhibited by monoclonal antibodies (mAb) directed at the CD11a/CD18
     molecule but not those reactive with other T cell surface molecules such
     as CD2, CD7, CD28, CD29 or CD49d.  None of these mAb, including
     anti-CD11a/CD18, had any effect on SAg-induced expression of
     IL-2 and IL-4 genes or SAg-induced [Ca2+]i response.  Addition
     of cytokines such as IL-1 alpha, IL-2, IL-4, IL-6, GM-CSF, IFN-gamma,
     tumor necrosis factor (TNF-alpha, or TNF-beta), or neutralizing Ab
     to these cytokines had no effect on SAg-induced death of
     Ag-specific TCL.  The T cells which survived the death-inducing effects of
     SAg showed down-regulation of the CD3/T cell receptor and
     up-regulation of CD2 and HLA-DR expression, and upon re-exposure to the
     same SAg upregulated expression of mRNA for IL-2 and IFN-gamma.
     Presentation of SAg by B7+ ICAM-1+ LFA-3+ DR+ professional APC
     was also able to induce the death of Ag-specific TCL.  Together these
     results suggest that the activation with SAg causes programmed
     death of Ag-specific TCL cells via a mechanism that requires late
     participation of the CD11a/CD18 molecule.


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     (FILE 'HOME' ENTERED AT 14:17:33 ON 07 OCT 2010)

     FILE 'REGISTRY' ENTERED AT 14:17:46 ON 07 OCT 2010
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L1           10 S CYCLOPAMINE

     FILE 'CAPLUS' ENTERED AT 14:17:55 ON 07 OCT 2010
L2          294 S L1
L3          160 S L2 AND (CANCER OR TUMOR OR NEOPLASM)
L4           48 S L3 AND APOPTOSIS
L5            2 S L4 AND PD<20010702
L6            2 DUP REM L5 (0 DUPLICATES REMOVED)
L7           10 S L3 AND AD<20010702
L8           10 DUP REM L7 (0 DUPLICATES REMOVED)

     FILE 'MEDLINE, EMBASE, BIOSIS' ENTERED AT 14:19:59 ON 07 OCT 2010

     FILE 'REGISTRY' ENTERED AT 14:20:05 ON 07 OCT 2010
                SET SMARTSELECT ON
L9          SEL L1 1- CHEM :      31 TERMS
                SET SMARTSELECT OFF

     FILE 'MEDLINE, EMBASE, BIOSIS' ENTERED AT 14:20:08 ON 07 OCT 2010
L10        7357 S L9
L11        7357 S L1 OR L10
L12        1644 S L11 AND (CANCER OR TUMOR OR NEOPLASM)
L13         495 S L12 AND PD<20010702
L14          29 S L13 AND APOPTOSIS
L15          15 DUP REM L14 (14 DUPLICATES REMOVED)

=> s l12 not sag
L16         893 L12 NOT SAG

=> s l13 and pd<20010702
L17         495 L13 AND PD<20010702

=> s l16 and pd<20010702
L18          14 L16 AND PD<20010702

=> dup rem l18
PROCESSING COMPLETED FOR L18
L19           8 DUP REM L18 (6 DUPLICATES REMOVED)

=> d l19 1-8 ibib abs

L19  ANSWER 1 OF 8     MEDLINE on STN                   DUPLICATE 1
ACCESSION NUMBER:   2002074749     MEDLINE
DOCUMENT NUMBER:    PubMed ID: 11748155
TITLE:              The Sonic Hedgehog-Gli pathway regulates dorsal brain
                    growth and tumorigenesis.
AUTHOR:             Dahmane N; Sanchez P; Gitton Y; Palma V; Sun T; Beyna M;
                    Weiner H; Ruiz i Altaba A
CORPORATE SOURCE:   Skirball Institute of Biomolecular Medicine, Developmental
                    Genetics Program and Department of Cell Biology, NYU School
                    of Medicine, 540 First Avenue, New York, NY 10016, USA.
SOURCE:             Development (Cambridge, England), (2001 Dec) Vol.
                    128, No. 24, pp. 5201-12.
                    Journal code: 8701744. ISSN: 0950-1991. L-ISSN: 0950-1991.
PUB. COUNTRY:       England: United Kingdom
DOCUMENT TYPE:      (IN VITRO)
                    Journal; Article; (JOURNAL ARTICLE)
                    (RESEARCH SUPPORT, NON-U.S. GOV'T)
                    (RESEARCH SUPPORT, U.S. GOV'T, P.H.S.)
LANGUAGE:           English
FILE SEGMENT:       Priority Journals
ENTRY MONTH:        200202
ENTRY DATE:          Entered STN: 25 Jan 2002
                     Last Updated on STN: 8 Feb 2002
                     Entered Medline: 7 Feb 2002
AB   The mechanisms that regulate the growth of the brain remain unclear.  We
     show that Sonic hedgehog (Shh) is expressed in a layer-specific manner in
     the perinatal mouse neocortex and tectum, whereas the Gli genes, which are
     targets and mediators of SHH signaling, are expressed in proliferative
     zones.  In vitro and in vivo assays show that SHH is a mitogen for
     neocortical and tectal precursors and that it modulates cell proliferation
     in the dorsal brain.  Together with its role in the cerebellum, our
     findings indicate that SHH signaling unexpectedly controls the development
     of the three major dorsal brain structures.  We also show that a variety
     of primary human brain tumors and tumor lines
     consistently express the GLI genes and that cyclopamine, a SHH
     signaling inhibitor, inhibits the proliferation of tumor cells.
     Using the in vivo tadpole assay system, we further show that misexpression
     of GLI1 induces CNS hyperproliferation that depends on the activation of
     endogenous Gli1 function.  SHH-GLI signaling thus modulates normal dorsal
     brain growth by controlling precursor proliferation, an evolutionarily
     important and plastic process that is deregulated in brain tumors
     .

L19  ANSWER 2 OF 8     MEDLINE on STN                   DUPLICATE 2
ACCESSION NUMBER:    2001328790     MEDLINE
DOCUMENT NUMBER:     PubMed ID: 11396162
TITLE:               Inhibitory effect of steroidal alkaloids on drug transport
                     and multidrug resistance in human cancer cells.
AUTHOR:              Lavie Y; Harel-Orbital T; Gaffield W; Liscovitch M
CORPORATE SOURCE:    Department of Biological Regulation, Weizmann Institute of
                     Science, Rehovot 76100, Israel.
SOURCE:              Anticancer research, (2001 Mar-Apr) Vol. 21, No.
                     2A, pp. 1189-94.
                     Journal code: 8102988. ISSN: 0250-7005. L-ISSN: 0250-7005.
PUB. COUNTRY:        Greece
DOCUMENT TYPE:       Journal; Article; (JOURNAL ARTICLE)
LANGUAGE:            English
FILE SEGMENT:        Priority Journals
ENTRY MONTH:         200107
ENTRY DATE:          Entered STN: 30 Jul 2001
                     Last Updated on STN: 30 Jul 2001
                     Entered Medline: 26 Jul 2001
AB   Intrinsic or acquired resistance of tumor cells to multiple
     cytotoxic drugs (multidrug resistance MDR) is a major cause of failure of
     cancer chemotherapy.  MDR is often caused by elevated expression
     of drug transporters such as P-glycoprotein (P-gp) or multidrug resistance
     protein (MRP).  A number of compounds, termed chemosensitizers, have
     little or no cytotoxic action of their own, but inhibit (P-gp) or
     MRP-mediated drug export and are capable of sensitizing MDR cells to the
     cytotoxic effects of chemotherapeutic drugs.  Here we examined the ability
     of steroidal alkaloids of plant origin, namely the Veratrum sp. alkaloid
     cyclopamine and the Lycopersicon sp. alkaloid tomatidine, to act
     as potent and effective chemosensitizers in multidrug resistant
     tumor cells.  Drug uptake was determined by measuring accumulation
     of tetramethylrosamine in multidrug resistant NCI AdrR human
     adenocarcinoma cells.  Resistance to adriamycin and vinblastine was
     determined by utilizing the MTT cell survival assay.  Cyclopamine
     and tomatidine elevate tetramethylrosamine uptake by NCI AdrR cells and
     sensitize the cells to the cytotoxic action of adriamycin and vinblastine.
     In both cases these agents are comparable in patency and efficacy to
     verapamil, a reversal agent commonly used in MDR research.  It is
     concluded that steroidal alkaloids of plant origin act as inhibitors of
     P-gp-mediated drug transport and multidrug resistance and therefore may
     serve as chemosensitizers in combination chemotherapy with conventional
     cytotoxic drugs for treating multidrug resistant cancer.

L19  ANSWER 3 OF 8     MEDLINE on STN                    DUPLICATE 3
ACCESSION NUMBER:   2000439367     MEDLINE
DOCUMENT NUMBER:    PubMed ID: 10984056
TITLE:              Effects of oncogenic mutations in Smoothened and Patched
                    can be reversed by cyclopamine.
AUTHOR:             Taipale J; Chen J K; Cooper M K; Wang B; Mann R K;
                    Milenkovic L; Scott M P; Beachy P A
CORPORATE SOURCE:   Department of Molecular Biology and Genetics, Howard Hughes
                    Medical Institute, The Johns Hopkins University School of
                    Medicine, Baltimore, Maryland 21205, USA.
SOURCE:             Nature, (2000 Aug 31) Vol. 406, No. 6799, pp.
                    1005-9.
                    Journal code: 0410462. ISSN: 0028-0836. L-ISSN: 0028-0836.
PUB. COUNTRY:       ENGLAND: United Kingdom
DOCUMENT TYPE:      Journal; Article; (JOURNAL ARTICLE)
                    (RESEARCH SUPPORT, NON-U.S. GOV'T)
LANGUAGE:           English
FILE SEGMENT:       Priority Journals
ENTRY MONTH:        200009
ENTRY DATE:         Entered STN: 28 Sep 2000
                    Last Updated on STN: 28 Sep 2000
                    Entered Medline: 21 Sep 2000
AB   Basal cell carcinoma, medulloblastoma, rhabdomyosarcoma and other human
     tumours are associated with mutations that activate the
     proto-oncogene Smoothened (SMO) or that inactivate the tumour
     suppressor Patched (PTCH).  Smoothened and Patched mediate the cellular
     response to the Hedgehog (Hh) secreted protein signal, and oncogenic
     mutations affecting these proteins cause excess activity of the Hh
     response pathway.  Here we show that the plant-derived teratogen
     cyclopamine, which inhibits the Hh response, is a potential
     'mechanism-based' therapeutic agent for treatment of these tumours
     .  We show that cyclopamine or synthetic derivatives with
     improved potency block activation of the Hh response pathway and abnormal
     cell growth associated with both types of oncogenic mutation.  Our results
     also indicate that cyclopamine may act by influencing the
     balance between active and inactive forms of Smoothened.

L19  ANSWER 4 OF 8     MEDLINE on STN
ACCESSION NUMBER:   2001059467     MEDLINE
DOCUMENT NUMBER:    PubMed ID: 11042037
TITLE:              Erythroid differentiation in vitro is blocked by
                    cyclopamine, an inhibitor of hedgehog signaling.
AUTHOR:             Detmer K; Walker A N; Jenkins T M; Steele T A; Dannawi H
CORPORATE SOURCE:   Division of Basic Medical Sciences, Mercer University
                    School of Medicine, Macon, Georgia 31207, USA..
                    detmer.k@gain.mercer.edu
SOURCE:             Blood cells, molecules & diseases, (2000 Aug)
                    Vol. 26, No. 4, pp. 360-72.
                    Journal code: 9509932. ISSN: 1079-9796. L-ISSN: 1079-9796.
PUB. COUNTRY:       United States
DOCUMENT TYPE:      Journal; Article; (JOURNAL ARTICLE)
                    (RESEARCH SUPPORT, NON-U.S. GOV'T)
LANGUAGE:           English
FILE SEGMENT:       Priority Journals
OTHER SOURCE:       GENBANK-AF130867
ENTRY MONTH:        200012
ENTRY DATE:         Entered STN: 22 Mar 2001
                    Last Updated on STN: 22 Mar 2001
                    Entered Medline: 22 Dec 2000
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AB   Adult hematopoietic differentiation is a developmental process that
     employs many of the same molecular mechanisms as embryogenesis.  To
     explore the possibility that hedgehog signaling is involved in the control
     of hematopoietic differentiation, we screened a panel of human leukemia
     cell lines for the expression of Patched1 and Smoothened, the receptor and
     coreceptor for hedgehog ligands.  Expression was found in multiple cell
     lines, and Patched1 expression was detected in normal marrow.  Induction
     of myeloid differentiation in cell lines downregulated expression of both
     genes.  When normal marrow mononuclear cells were grown in semisolid
     medium in the presence of 10 microM cyclopamine, development of
     colonies of granulocytic/monocytic lineage was unaffected in terms of both
     number and morphology.  The number of erythroid colonies, however, was
     significantly reduced (P < 0.01).  Furthermore, hemoglobinization was
     substantially delayed relative to controls in those erythroid colonies
     that did form.  Incubation of hematopoietic progenitors with Shh-N and
     GM-CSF resulted in increased granulocyte/monocyte colonies (P < 0.01); the
     increase was blocked by cyclopamine.  Incubation of
     hematopoietic progenitors with Shh-N and stem cell factor resulted in
     larger erythroid colonies.  These results suggest that elements of the
     hedgehog signaling pathway are involved in the control of hematopoietic
     differentiation.
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L19  ANSWER 5 OF 8  BIOSIS  COPYRIGHT (c) 2010 The Thomson Corporation  on STN
ACCESSION NUMBER:    2000:358663  BIOSIS
DOCUMENT NUMBER:     PREV200000358663
TITLE:               Erythroid differentiation in vitro is blocked by
                     cyclopamine, an inhibitor of hedgehog signaling.
AUTHOR(S):           Detmer, K. [Reprint author]; Walker, A. N. [Reprint
                     author]; Jenkins, T. M.; Steele, T. A. [Reprint author];
                     Dannawi, H.
CORPORATE SOURCE:    Mercer University School of Medicine, Macon, GA, 31201, USA
SOURCE:              Developmental Biology, (June 1, 2000) Vol. 222,
                     No. 1, pp. 242. print.
                     Meeting Info.: Fifty-ninth Annual Meeting of the Society
                     for Developmental Biology. Boulder, Colorado, USA. June
                     07-11, 2000. Society for Developmental Biology.
                     CODEN: DEBIAO. ISSN: 0012-1606.
DOCUMENT TYPE:       Conference; (Meeting)
                     Conference; Abstract; (Meeting Abstract)
LANGUAGE:            English
ENTRY DATE:          Entered STN: 16 Aug 2000
                     Last Updated on STN: 8 Jan 2002

L19  ANSWER 6 OF 8  BIOSIS  COPYRIGHT (c) 2010 The Thomson Corporation  on STN
ACCESSION NUMBER:    2000:233990  BIOSIS
DOCUMENT NUMBER:     PREV200000233990
TITLE:               Indian Hedgehog and Parathyroid hormone related protein
                     signaling in cartilage tumors of bone.
AUTHOR(S):           Hopyan, Sevan [Reprint author]; Gokgoz, Nalan [Reprint
                     author]; Poon, Raymond [Reprint author]; Bell, Robert S.
                     [Reprint author]; Andrulis, Irene L. [Reprint author];
                     Wunder, Jay S. [Reprint author]; Alman, Benjamin A.
                     [Reprint author]
CORPORATE SOURCE:    Univ of Toronto, Toronto, ON, Canada
SOURCE:              Proceedings of the American Association for Cancer Research
                     Annual Meeting, (March, 2000) No. 41, pp. 206.
                     print.
                     Meeting Info.: 91st Annual Meeting of the American
                     Association for Cancer Research. San Francisco, California,
                     USA. April 01-05, 2000.
                     ISSN: 0197-016X.
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DOCUMENT TYPE:      Conference; (Meeting)
                    Conference; Abstract; (Meeting Abstract)
LANGUAGE:           English
ENTRY DATE:         Entered STN: 7 Jun 2000
                    Last Updated on STN: 5 Jan 2002

L19  ANSWER 7 OF 8  BIOSIS  COPYRIGHT (c) 2010 The Thomson Corporation  on STN
ACCESSION NUMBER:   2000:211718  BIOSIS
DOCUMENT NUMBER:    PREV200000211718
TITLE:              Inhibition of prostate morphogenesis by the Sonic hedgehog
                    pathway inhibitor cyclopamine.
AUTHOR(S):          Berman, David M. [Reprint author]; Chen, James K. [Reprint
                    author]; Beachy, Philip A. [Reprint author]
CORPORATE SOURCE:   Baltimore, MD, USA
SOURCE:             Journal of Urology, (April, 2000) Vol. 163, No. 4
                    Suppl., pp. 204. print.
                    Meeting Info.: 95th Annual Meeting of the American
                    Urological Association, Inc. Atlanta, Georgia, USA. April
                    29, 2000-May 04, 1999.
                    CODEN: JOURAA. ISSN: 0022-5347.
DOCUMENT TYPE:      Conference; (Meeting)
                    Conference; Abstract; (Meeting Abstract)
                    Conference; (Meeting Poster)
LANGUAGE:           English
ENTRY DATE:         Entered STN: 24 May 2000
                    Last Updated on STN: 5 Jan 2002

L19  ANSWER 8 OF 8     MEDLINE on STN                    DUPLICATE 4
ACCESSION NUMBER:   1999102111     MEDLINE
DOCUMENT NUMBER:    PubMed ID: 9882493
TITLE:              Essential role for Sonic hedgehog during hair follicle
                    morphogenesis.
AUTHOR:             Chiang C; Swan R Z; Grachtchouk M; Bolinger M; Litingtung
                    Y; Robertson E K; Cooper M K; Gaffield W; Westphal H;
                    Beachy P A; Dlugosz A A
CORPORATE SOURCE:   Laboratory of Mammalian Genes and Development, National
                    Institutes of Health, Bethesda, Maryland, 20892, USA.
SOURCE:             Developmental biology, (1999 Jan 1) Vol. 205, No.
                    1, pp. 1-9.
                    Journal code: 0372762. ISSN: 0012-1606. L-ISSN: 0012-1606.
PUB. COUNTRY:       United States
DOCUMENT TYPE:      Journal; Article; (JOURNAL ARTICLE)
LANGUAGE:           English
FILE SEGMENT:       Priority Journals
ENTRY MONTH:        199902
ENTRY DATE:         Entered STN: 23 Feb 1999
                    Last Updated on STN: 23 Feb 1999
                    Entered Medline: 5 Feb 1999
AB   The hair follicle is a source of epithelial stem cells and site of origin
     for several types of skin tumors.  Although it is clear that
     follicles arise by way of a series of inductive tissue interactions,
     identification of the signaling molecules driving this process remains a
     major challenge in skin biology.  In this study we report an obligatory
     role for the secreted morphogen Sonic hedgehog (Shh) during hair follicle
     development.  Hair germs comprising epidermal placodes and associated
     dermal condensates were detected in both control and Shh -/- embryos, but
     progression through subsequent stages of follicle development was blocked
     in mutant skin.  The expression of Gli1 and Ptc1 was reduced in Shh -/-
     dermal condensates and they failed to evolve into hair follicle papillae,
     suggesting that the adjacent mesenchyme is a critical target for
     placode-derived Shh.  Despite the profound inhibition of hair follicle
     morphogenesis, late-stage follicle differentiation markers were detected
     in Shh -/- skin grafts, as well as cultured vibrissa explants treated with
     cyclopamine to block Shh signaling.  Our findings reveal an
     essential role for Shh during hair follicle morphogenesis, where it is
     required for normal advancement beyond the hair germ stage of development.
     Copyright 1999 Academic Press.


=> d his

     (FILE 'HOME' ENTERED AT 14:17:33 ON 07 OCT 2010)

     FILE 'REGISTRY' ENTERED AT 14:17:46 ON 07 OCT 2010
L1           10 S CYCLOPAMINE

     FILE 'CAPLUS' ENTERED AT 14:17:55 ON 07 OCT 2010
L2          294 S L1
L3          160 S L2 AND (CANCER OR TUMOR OR NEOPLASM)
L4           48 S L3 AND APOPTOSIS
L5            2 S L4 AND PD<20010702
L6            2 DUP REM L5 (0 DUPLICATES REMOVED)
L7           10 S L3 AND AD<20010702
L8           10 DUP REM L7 (0 DUPLICATES REMOVED)

     FILE 'MEDLINE, EMBASE, BIOSIS' ENTERED AT 14:19:59 ON 07 OCT 2010

     FILE 'REGISTRY' ENTERED AT 14:20:05 ON 07 OCT 2010
                SET SMARTSELECT ON
L9          SEL L1 1- CHEM :      31 TERMS
                SET SMARTSELECT OFF

     FILE 'MEDLINE, EMBASE, BIOSIS' ENTERED AT 14:20:08 ON 07 OCT 2010
L10        7357 S L9
L11        7357 S L1 OR L10
L12        1644 S L11 AND (CANCER OR TUMOR OR NEOPLASM)
L13         495 S L12 AND PD<20010702
L14          29 S L13 AND APOPTOSIS
L15          15 DUP REM L14 (14 DUPLICATES REMOVED)
L16         893 S L12 NOT SAG
L17         495 S L13 AND PD<20010702
L18          14 S L16 AND PD<20010702
L19           8 DUP REM L18 (6 DUPLICATES REMOVED)

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---Logging off of STN---



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Executing the logoff script...


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COST IN U.S. DOLLARS                             SINCE FILE      TOTAL
                                                      ENTRY    SESSION
FULL ESTIMATED COST                                   28.40     105.99

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)       SINCE FILE      TOTAL
                                                      ENTRY    SESSION
CA SUBSCRIBER PRICE                                     0.00     -10.20
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STN INTERNATIONAL LOGOFF AT 14:29:32 ON 07 OCT 2010
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